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We wish to respond to Dr. Rockhill's comments on the paper by Gail and Pfeiffer (2005).

Dr. Rockhill's first point was that "the dichotomy between screening and preventive intervention seems somewhat artificial and arbitrary." We believe she misconstrued colonoscopy as the screening procedure, leading to subsequent confusion. To define a statistical framework for assessing the performance of risk models, we differentiated between a pure screening procedure, defined as an action that does not in itself change the probability of the outcome, and an intervention, defined as an action that does change the probability of disease. As Dr. Rockhill points out, colonoscopy falls into the second category, because removing colon polyps lowers the subsequent risk of colon cancer risk. **The screening procedure we considered (page 233) was not colonoscopy, but rather determining colon cancer risk from a self-administered questionnaire.** Based on the risk estimate, the decision was whether to further evaluate the person with colonoscopy or to defer that evaluation. The questionnaire-based risk screen clearly falls into the category of events that do not change the probability of outcome. The assumption that was implicit in the cost structure of the screening example is that diagnosing a cancer early is less costly than diagnosing a cancer in later stages, which led to the cost of 11 for those who are destined to develop colon cancer and are referred for colonoscopy compared to a cost of 100 for those who are destined to develop colon cancer but are not referred for colonoscopy.

The misunderstanding of our screening procedure explains the second comment on the "seeming inconsistency" between the example of screening versus the example of intervention. It also explains the third comment about the cost structure for tamoxifen intervention. The costs for tamoxifen intervention were chosen to reflect the fact that both invasive breast cancer and stroke are life threatening. They were therefore assigned large equal costs, compared to which the costs of taking tamoxifen were negligible. We pointed out that a full accounting would consider other risks and benefits of tamoxifen (see Gail *et al.*, 1999) and stated, "For ease of exposition, we consider only two outcomes and use the terminology of invasive breast cancer and stroke, but the ideas extend to multiple outcomes."

We fully agree with Dr. Rockhill's final comment: "However, the conclusion one comes to about the importance of discriminatory accuracy is highly dependent on the assumed structure of the relative costs." Indeed, our examples illustrate this point and show that high discriminatory power can be crucial for some applications but not others.

References

1. Gail M.H. and Pfeiffer R.M. (2005). On criteria for evaluating models of absolute risk. *Biostatistics* **6**, 227-239.

2. Gail M.H., Costantino J.P., Bryant J., Croyle R., Freedman L., Helzlsouer K., and Vogel V. (1999). Weighing the risks and benefits of tamoxifen treatment for preventing breast cancer. *Journal of the National Cancer Institute* **91,**1829-1846.

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